

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

Claims 100 – 143 (canceled).

Claim 144 (currently amended) A method of regulating ~~a transient~~ expression of a desired protein or RNA in ~~an~~ a non-human animal *in vivo*, the method comprising:

administering to the animal a pharmacological dose of a ligand, wherein the ligand is an antagonist for a non-mutated steroid hormone receptor protein,

wherein the animal comprises:

(a) ~~a first nucleic acid cassette comprising a coding sequence of~~ encoding a molecular switch comprising a mutated receptor protein, wherein the mutated receptor protein comprises:

a non-steroid hormone receptor DNA binding domain which binds a promoter that is transcriptionally linked to a target gene;

a mutated steroid hormone receptor superfamily ligand binding domain which is distinct from a naturally occurring ligand binding domain, has an alternation in C-terminal amino acids and binds the ligand by one or more alternations that reverse a ligand specificity of the receptor and confer activation by the antagonist;

a transactivation domain which causes a transcription from the promoter when the molecular switch is bound to the promoter and the ligand; and

(b) ~~a second nucleic acid cassette comprising the target gene transcriptionally linked to the promoter,~~

wherein administration of the ligand regulates expression of the desired protein or RNA in the animal from the target gene.

Claim 145 (previously presented) The method of claim 144, wherein the mutated steroid hormone superfamily receptor ligand binding domain is selected from the group consisting of estrogen, progesterone, androgen, Vitamin D, COUP-TF, cis-retinoic acid, Nurr-1, thyroid hormone, mineralocorticoid, glucocorticoid-alpha, glucocorticoid-beta, and orphan receptor ligand binding domains.

Claim 146 (currently amended) The method of claim 144 wherein the mutated receptor protein is a mutated progesterone receptor ~~and the DNA binding domain is a non-steroid hormone DNA binding domain.~~

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Claim 147 (currently amended) The method of claim 144, wherein the ~~first nucleic acid cassette and the second nucleic acid cassette in the animal are on separate plasmids~~ target gene and promoter are encoded on a nucleic acid cassette that has been introduced into the animal.

Claim 148 (currently amended) The method of claim 144, wherein the non-steroid hormone receptor DNA binding domain is a natural DNA binding domain, a non-native DNA binding domain, or, a modified DNA binding domain.

Claim 149 (currently amended) The method of claim 144, wherein the animal is a transgenic mammal.

Claim 150 (currently amended) The method of claim ~~149~~ 144, wherein the ~~mammal is a human transgenic~~ nucleic acid encoding the molecular switch has been introduced into the animal on an expression vector that encodes the molecular switch.

Claim 151 (previously presented) The method of claim 144, wherein the DNA binding domain is a Gal-4 DNA binding domain.

Claim 152 (currently amended) The method of claim 144, wherein the mutated steroid hormone receptor ligand binding domain binds a compound selected from the group consisting of 5 α -pregnane-3, 20-dione; 11 β -(4-dimethylaminophenyl)-17 β -hydroxy-17 α -propinyl-4, 9-estradiene-3-one; 11 β -(4-dimethylaminophenyl)-17 α -hydroxy-17 β -(3-hydroxypropyl)-13 α -methyl-4,9-gonadiene-3-one; 11 β -(4-acetylphenyl)-17 β -hydroxy-17 α -(1-propinyl)-4,9-estradiene-3-one; 11 β -(4-dimethylaminophenyl)-17 β -hydroxy-17 α -(3-hydroxy-1 (Z)-propenyl-estra-4, 9-diene-3-one; (7 β ,11 β ,17 β)-11-(4-dimethylaminophenyl)-7-methyl-4', 5'-dihydrospiro(ester-4, 9-diene-17, 2' (3'H)-furan)-3-one; (11 β ,14 β ,17 α)-4',5'-dihydro-11-(4-dimethylaminophenyl)-(spiroestra-4,9-diene-17,2'(3'H)-furan)-3-one.

153 (previously presented) The method of claim 144, wherein the mutated steroid hormone superfamily receptor ligand binding domain binds to a compound selected from the group consisting of non-natural ligands, non-native hormones and anti-hormones.

Claim 154 (previously presented) The method of claim 144, wherein the DNA binding domain is a GAL-4 DNA binding domain, a virus DNA binding domain, an insect DNA binding domain, or a non-mammalian DNA binding domain.

Claim 155 (previously presented) The method of claim 144, wherein the transactivation domain is selected from the group consisting of VP-16, TAF-1, TAF-2, and TAU-2.

Claim 156 (previously presented) The method of claim 155, wherein the transactivation domain comprises a TAF-1 transactivation domain.

Claim 157 (previously presented) The method of claim 155, wherein the transactivation domain is a VP-16 transactivation domain and wherein the DNA binding domain is a GAL-4 DNA binding domain.

Claim 158 (previously presented) The method of claim 155, wherein the transactivation domain is a TAF-1 transactivation domain and wherein the DNA binding domain is a GAL-4 binding domain.

Claim 159 (previously presented) The method of claim 144, wherein the molecular switch is tissue specific.

Claim 160 (previously presented) The method of claim 159, wherein the tissue specificity of the molecular switch is controlled by a tissue-specific transactivation domain.

Claim 161 (currently amended) The method of claim ~~159~~ 147, wherein the ~~second nucleic acid cassette comprising the target gene and promoter~~ are encoded in a nucleic acid cassette that further comprises a tissue-specific cis-element.

Claim 162 (currently amended) The method of claim ~~144~~ 146, wherein the alternation is ~~a deletion of in from about 1 to about 54 naturally occurring~~ carboxyl terminal amino acids in the ~~mutated steroid hormone receptor superfamily~~ progesterone receptor ligand binding domain.

Claim 163 (previously presented) The method of claim 144, wherein the ligand is RU38486.

Claim 164 (previously presented) The method of claim 144, wherein the ligand is 11 beta-(4-dimethylaminophenyl)-17 beta-hydroxy-17 alpha-propinyl-4, 9-estradiene-3-one.

Claim 165 (currently amended) The method of claim ~~144~~ 146, wherein the ligand is an antiprogestosterone.

Claim 166 (previously presented) The method of claim 144, wherein the ligand requires conversion to an active form in an end organ.

Claim 167 (previously presented) The method of claim 144, wherein the ligand has a side chain which increases or restricts solubility, membrane transfer or target organ accessibility.

Claim 168 (currently amended) A method of regulating ~~an transient~~ expression of a ~~desired protein or RNA target gene~~ in an animal *in vivo* comprising:

administering to the animal a pharmacological dose of a ligand that activates a molecular switch encoded by a ~~molecule~~ molecular switch expression cassette, the cassette having been previously administered to the animal for transient expression or is comprised in a non-human transgenic animal ~~comprised in the animal~~, wherein the molecular switch comprises a sequence specific non-steroid hormone receptor DNA binding domain and mutated steroid hormone superfamily receptor ligand binding domain which is characterized by alteration of from about 1 to about 120 naturally occurring C-terminal amino acids of the ligand binding domain of a corresponding wild type steroid hormone superfamily receptor and is activated by the ligand which is not a native ligand for the corresponding wild type steroid hormone superfamily receptor ~~ligand-binding domain~~ and wherein the activation of the molecular switch results in binding to a specific DNA sequence in the regulatory region of a target gene promoter and ~~results in the expression of the desired protein or RNA~~ from the target gene.

Claim 169 (previously presented) The method of claim 168, wherein the mutated steroid hormone superfamily receptor ligand binding domain is the ligand binding domain of a steroid hormone superfamily receptor selected from the group consisting of: estrogen; progesterone; glucocorticoid- α ; glucocorticoid- β ; mineralcorticoid; androgen; thyroid hormone; retinoic acid; retinoid X; Vitamin D; COUP-TF; ecdysone; Nurr-1 and orphan receptors.

Claim 170 (previously presented) The method of claim 168, wherein the mutated steroid hormone superfamily receptor ligand binding domain is a mutated progesterone ligand binding domain and the ligand is an anti-progestin.

Claim 171 (previously presented) The method of claim 170, wherein the anti-progestin is selected from the group consisting of: RU 38486; Org31806; and Org 31376.

Claim 172 (previously presented) The method of claim 168, wherein DNA binding domain is a non-steroid hormone DNA binding domain.

Claim 173 (currently amended) The method of claim 168, wherein the DNA binding domain is selected from the group consisting of: a GAL-4 DNA binding domain; a viral DNA binding domain[[s]]; an insect DNA binding domain[[s]]; and a non-mammalian DNA binding domains.

Claim 174 (previously presented) The method of claim 168, wherein the molecular switch further comprises a transactivation domain distinct from a steroid hormone receptor superfamily transactivation domain.

Claim 175 (previously presented) The method of claim 168, wherein the transient expression is up-regulated.

Claim 176 (currently amended) The method of claim ~~135~~ 168, wherein the transient expression is down-regulated.

Claim 177 (currently amended) A method of regulating a transient expression of a desired protein or RNA in an animal *in vivo*, the method comprising:

administering to the animal a pharmacological dose of a ligand, wherein the ligand is an antagonist for a non-mutated progesterone receptor protein,

wherein the animal ~~comprises~~ has been previously administered a coding sequence of a molecular switch comprising a mutated progesterone receptor protein, wherein the mutated progesterone receptor protein comprises:

a DNA binding domain specific for a DNA site on a promoter transcriptionally linked to a target gene;

a mutated progesterone receptor ligand binding domain which has ~~a deletion~~ alterations of from 1 to 54 naturally occurring C-terminal amino acids and ~~binds to and~~ is activated by the ligand;

a transactivation domain which causes a transcription from the promoter when the molecular switch is bound to the promoter and the ligand; and

wherein administration of the ligand regulates expression of the desired protein or RNA from the target gene.

Claim 178 (previously presented) The method of claim 177, wherein the DNA binding domain is a natural DNA binding domain, a non-native DNA binding domain, or a modified DNA binding domain.

Claim 179 (previously presented) The method of claim 177, wherein the DNA binding domain is a GAL-4 DNA binding domain, a virus DNA binding domain, an insect DNA binding domain, or a non-mammalian DNA binding domain.

Claim 180 (previously presented) The method of claim 177, wherein the animal is a mammal.

Claim 181 (previously presented) The method of claim 180, wherein the mammal is a human.

Claim 182 (currently amended) The method of claim 177, wherein the ligand selected from the group consisting of 5 α -pregnane-3,20-dione; 11 β -(4-dimethylaminophenyl)-17 β -hydroxy-17 α -propinyl-4,9-estradiene-3-one; 11 β -(4-dimethylaminophenyl)-17 α -hydroxy-17 β -(3-hydroxypropyl)-13 α -methyl-4,9-gonadiene-3-one; 11 β -(4-acetylphenyl)-17 β -hydroxy-17 α [[β]]-(1-propinyl)-4,9-estradiene-3-one; 11 β -(4-dimethylaminophenyl)-17 β -hydroxy-17[[β]] α [[β]](3-hydroxy-1 (Z)-propenyl-estra-4,9-diene-3-one; (7 β ,11 β ,17 β)-11-(4-dimethylaminophenyl)-7-methyl-4',5'-dihydrospiro(ester-4,9-diene-17,2'(3'H)-furan)-3-one; (11 β ,14 β ,17 α)-4',5'-dihydro-11-(4-dimethylaminophenyl)- (spiroestra-4,9-diene-17,2'(3'H)-furan)-3-one.

Claim 183 (previously presented) The method of claim 177 wherein the ligand is an anti-progesterone.

Claim 184 (currently amended) The method of claim 183 wherein the antiprogestosterone is RU 34846, Org ~~3486~~ 31806, or Org 31376.

Claim 185 (previously presented) The method of claim 177, wherein the mutated progesterone receptor ligand binding domain binds to a compound selected from the group consisting of non-natural ligands, non-native hormones and anti-hormones.

Claim 186 (previously presented) The method of claim 177, wherein the transactivation domain is selected from the group consisting of VP-16, TAF-1, TAF-2, and TAU-2.

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Claim 187 (previously presented) The method of claim 177, wherein the transactivation domain is a VP-16 transactivation domain and wherein the DNA binding domain is a GAL-4 DNA binding domain.

Claim 188 (previously presented) The method of claim 177, wherein the transactivation domain is a TAF-1 transactivation domain and wherein the DNA binding domain is a GAL-4 binding domain.

Claim 189 (previously presented) The method of claim 177, wherein the molecular switch is tissue specific.

Claim 190 (previously presented) The method of claim 189, wherein the tissue specificity of the molecular switch is controlled by a tissue-specific transactivation domain.

Claim 191 (previously presented) The method of claim 190, wherein the target gene further comprises a tissue-specific cis-element.

Claim 192 (previously presented) The method of claim 177, wherein the ligand has a side chain which increases or restricts solubility, membrane transfer or target organ accessibility.